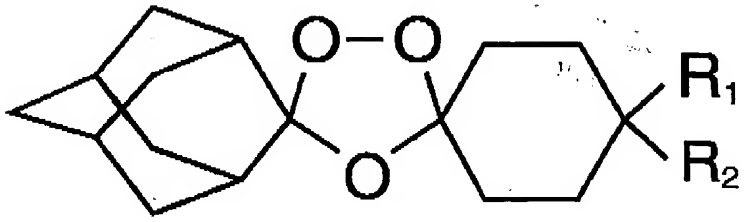
Amendments to the Claims

Claim 1 (Previously presented): A spiro or dispiro 1,2,4-trioxolane having the following structure:



wherein R_1 and R_2 are the same or different, and are selected from the group consisting of hydrogen, substituted or unsubstituted linear or branched alkyl, aryl, and alkaryl groups and substituted or unsubstituted alicyclic groups that are optionally interrupted by one or more oxygen, sulfur or nitrogen atoms, substituted or unsubstituted aromatic or heterocyclic groups that may be interrupted by one or more oxygen, sulfur or nitrogen atoms, a hydroxy group, and a halogen, and further providing that the spirocyclohexyl ring attaching R_1 and R_2 are optionally interrupted by one or more oxygen, sulfur, or nitrogen atoms.

Claim 2 (Original): The trioxolane of claim 1 whereby R_1 is hydrogen and R_2 is $(CH_2)_n$-Y; whereby Y is a functional group selected from the group consisting of an alkyl, ketone, acid, alcohol, amine, amide, sulfonamide, guanidine, ether, ester, oxime, urea, oxime ether, sulfone, lactone, carbamate, semicarbazone, phenyl, and heterocycle; and n is an integer.

Claim 3 (Previously presented): The trioxolane of claim 2 whereby Y is a non-acidic functional group.

Claim 4 (Previously presented): The trioxolane of claim 3 whereby Y is a weak base.

Claim 5 (Canceled).

Claim 6 (Original): The trioxolane of claim 2 whereby n = 1.

Claim 7 (Original): The spiro or dispiro 1,2,4-trioxolane of claim 1 wherein the 1,2,4-trioxolane is selected from the group consisting of OZ271, OZ277, OZ281, OZ279, OZ288, OZ289, OZ290, OZ296, OZ297, OZ298, OZ301, OZ305, OZ309, OZ315, OZ317, OZ319, OZ320, OZ323, OZ329, OZ333, OZ335, OZ336, OZ337, OZ338, and OZ339.

Claim 8 (Original): The spiro or dispiro 1,2,4-trioxolane of claim 7 wherein the 1,2,4-trioxolane is selected from the group consisting of OZ271, OZ277, OZ279, OZ301, OZ305, OZ315, OZ317, OZ319, OZ323, OZ329, OZ338, and OZ339.

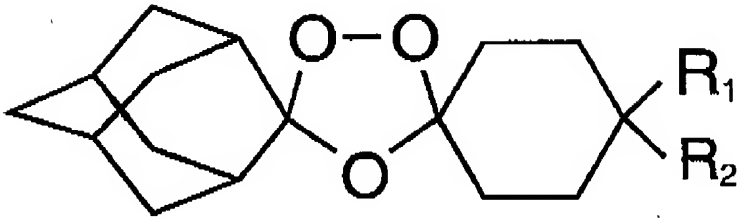
Claim 9 (Original): *Cis*-adamantane-2-spiro-3'-8'-[[[(2'-amino-2'-methylpropyl)amino]carbonyl]methyl]-1',2',4'-trioxaspiro[4.5]decane *p*-tosylate.

Claim 10 (Original): *Cis*-adamantane-2-spiro-3'-8'-[(1'-piperazinylcarbonyl)methyl]-1',2',4'-trioxaspiro[4.5]decane *p*-tosylate.

Claim 11 (Original): *Cis*-Adamantane-2-spiro-3'-8'-[[(1'-piperazinylcarbonyl)amino]methyl]-1',2',4'-trioxaspiro[4.5]decane *p*-tosylate.

Claim 12 (Original): *Cis*-Adamantane-2-spiro-3'-8'-[[(4'-amino-1'-piperidinyl)carbonyl]methyl]-1',2',4'-trioxaspiro[4.5]decane *p*-tosylate.

Claim 13 (Previously presented): A pharmaceutical composition for prophylaxis and treatment of malaria comprising: a malaria prophylaxis or malaria treatment-effective amount of a spiro or dispiro 1,2,4-trioxolane, its prodrugs and optical isomers thereof, and a pharmaceutically acceptable carrier, said trioxolane having the following structure:



wherein R_1 and R_2 are the same or different, and are selected from the group consisting of hydrogen, substituted or unsubstituted linear or branched alkyl, aryl, and alkaryl groups and substituted or unsubstituted alicyclic groups that are optionally interrupted by one or more oxygen, sulfur or nitrogen atoms, substituted or unsubstituted aromatic or heterocyclic groups that may be interrupted by one or more oxygen, sulfur or nitrogen atoms, a hydroxy group, and a halogen, and further providing that the spirocyclohexyl ring attaching R_1 and R_2 are optionally interrupted by one or more oxygen, sulfur, or nitrogen atoms.

Claim 14 (Original): The pharmaceutical composition of claim 13 whereby R_1 is hydrogen and R_2 is $(CH_2)_n$-Y; whereby Y is a functional group selected from the group consisting of an alkyl, ketone, acid, alcohol, amine, amide, sulfonamide, guanidine, ether, ester, oxime, urea, oxime ether, sulfone, lactone, carbamate, semicarbazone, phenyl, and heterocycle; and n is an integer.

Claim 15 (Original): The pharmaceutical composition of claim 14 whereby Y is a non-acidic functional group.

Claim 16 (Original): The pharmaceutical composition of claim 14 whereby Y is a weak base.

Claim 17 (Original): The pharmaceutical composition of claim 16 whereby Y is an amide.

Claim 18 (Original): The pharmaceutical composition of claim 14 whereby n = 1.

Claim 19 (Original): The pharmaceutical composition of claim 13 wherein the trioxolane is selected from the group consisting of OZ271, OZ277, OZ281, OZ279, OZ288, OZ289, OZ290,

OZ296, OZ297, OZ298, OZ301, OZ305, OZ309, OZ315, OZ317, OZ319, OZ320, OZ323, OZ329, OZ333, OZ335, OZ336, OZ337, OZ338, and OZ339.

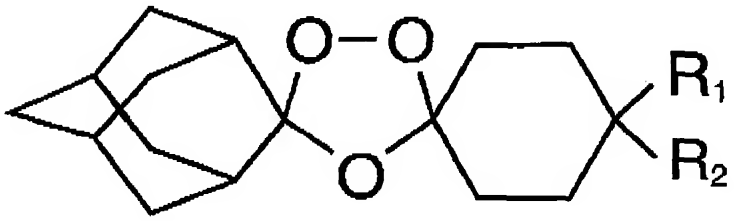
Claim 20 (Original): The pharmaceutical composition of claim 19 wherein the trioxolane is selected from the group consisting of OZ271, OZ277, OZ279, OZ301, OZ305, OZ315, OZ317, OZ319, OZ323, OZ329, OZ338, and OZ339.

Claim 21 (Original): The pharmaceutical composition of claim 13 wherein the 1,2,4-trioxolane is *cis*-adamantane-2-spiro-3'-8'-[[[(2'-amino-2'-methylpropyl)amino]carbonyl]methyl]-1',2',4'-trioxaspiro[4.5]decane *p*-tosylate.

Claim 22 (Original): The pharmaceutical composition of claim 13 wherein the 1,2,4-trioxolane is *cis*-adamantane-2-spiro-3'-8'-[(1'-piperazinylcarbonyl)methyl]-1',2',4'-trioxaspiro[4.5]decane *p*-tosylate.

Claim 23 (Original): The pharmaceutical composition of claim 13 that is suitable for administration by a method selected from the group consisting of oral, subcutaneous, intravenous, intranasal, rectal, sublingual, and buccal.

Claim 24 (Previously presented): A method of preventing or treating malaria comprising: administrating a malaria prevention or malaria treatment effective amount of a spiro or dispiro 1,2,4-trioxolane in a pharmaceutically acceptable carrier, said trioxolane having the following structure:



wherein R_1 and R_2 are the same or different, and are selected from the group consisting of hydrogen, substituted or unsubstituted linear or branched alkyl, aryl, and alkaryl groups and substituted or unsubstituted alicyclic groups that are optionally interrupted by one or more oxygen, sulfur or nitrogen atoms, substituted or unsubstituted aromatic or heterocyclic groups that are optionally interrupted by one or more oxygen, sulfur or nitrogen atoms, a hydroxy group, and a halogen, and further providing that the spirocyclohexyl ring attaching R_1 and R_2 may be interrupted by one or more oxygen, sulfur, or nitrogen atoms.

Claim 25 (Original): The method of claim 24 whereby R_1 is hydrogen and R_2 is $(CH_2)_n$-Y; whereby Y is a functional group selected from the group consisting of an alkyl, ketone, acid, alcohol, amine, amide, sulfonamide, guanidine, ether, ester, oxime, urea, oxime ether, sulfone, lactone, carbamate, semicarbazone, phenyl, and heterocycle; and n is an integer.

Claim 26 (Original): The method of claim 24 wherein the trioxolane is administered in a dose of between about 0.1-1000 mg/kg/day.

Claim 27 (Original): The method of claim 26 wherein the trioxolane is administered in a dose of between about 1-100 mg/kg/day.

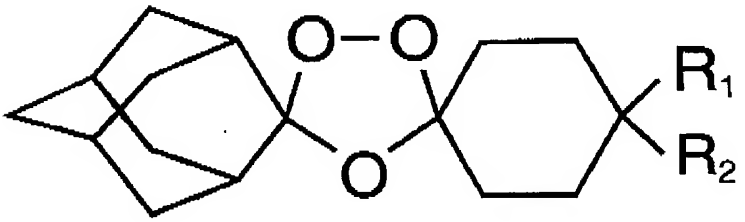
Claim 28 (Original): The method of claim 24 wherein the trioxolane is administered in a single dose.

Claim 29 (Original): The method of claim 24 wherein the trioxolane is administered in divided doses.

Claim 30 (Original): The method of claim 24 wherein the trioxolane is administered in a malaria-preventive dose beginning 1-2 weeks prior to malaria exposure and ending 1-2 weeks post exposure.

Claim 31 (Original): A method of claim 24 wherein the trioxolane is administered in a malaria-curative dose over 1-10 days.

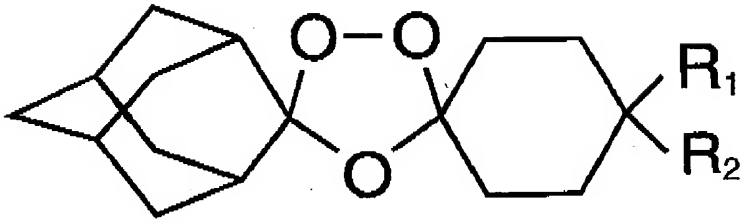
Claim 32 (Previously presented): A method of manufacturing a composition for prophylaxis and treatment of malaria comprising: mixing a malaria prophylaxis or malaria treatment-effective amount of a spiro or dispiro 1,2,4-trioxolane, its prodrugs and optical isomers thereof, with a pharmaceutically acceptable carrier, said trioxolane having the following structure:



wherein R_1 and R_2 are the same or different, and are selected from the group consisting of hydrogen, substituted or unsubstituted linear or branched alkyl, aryl, and alkaryl groups and substituted or unsubstituted alicyclic groups that are optionally interrupted by one or more oxygen, sulfur or nitrogen atoms, substituted or unsubstituted aromatic or heterocyclic groups that are optionally interrupted by one or more oxygen, sulfur or nitrogen atoms, a hydroxy group, and a halogen, and further providing that the spirocyclohexyl ring attaching R_1 and R_2 may be interrupted by one or more oxygen, sulfur, or nitrogen atoms.

Claim 33 (Canceled).

Claim 34 (Currently Amended): A method of prophylaxis or treatment of schistosomiasis comprising: administering a schistosomiasis prophylaxis or treatment effective amount or a spiro or dispiro 1,2,4-trioxolane in a pharmaceutically acceptable carrier, said trioxolane having the following structure:



wherein R_1 and R_2 are the same or different, and are selected from the group consisting of hydrogen, substituted or unsubstituted linear or branched alkyl, aryl, and alkaryl groups and substituted or unsubstituted alicyclic groups that are optionally interrupted by one or more oxygen, sulfur or nitrogen atoms, substituted or unsubstituted aromatic or heterocyclic groups that are optionally interrupted by one or more oxygen, sulfur or nitrogen atoms, a hydroxy group, and a halogen, and further providing that the spirocyclohexyl ring attaching R_1 and R_2 may be interrupted by one or more oxygen, sulfur, or nitrogen atoms.

Claim 35 (Canceled).

Claim 36 (Previously presented): The method of claim 57 wherein the trioxolane has a ketone or an aldehyde functional group, and is treated with an oxidizing agent to form a lactone or an acid.

Claim 37 (Original): The method of claim 36 wherein the trioxolane has a ketone or an aldehyde functional group and is treated with a reducing agent to form an amine or an alcohol.

Claim 38 (Original): The method of claim 36 wherein the trioxolane has a ketone or an aldehyde functional group, and is treated with a hydroxylamine or a hydrazine to form an oxime ether or a hydrazone, respectively.

Claim 39 (Previously presented): The method of claim 57 wherein the trioxolane has a ketone or an aldehyde functional group, and is treated with one or more diols and/or alcohols to form a ketal or acetal.

Claim 40 (Original): The method of claim 36 whereby the trioxolane is OZ05.

Claim 41 (Original): The method of claim 40 whereby OZ05 is treated with a heteroaryllithium, aryllithium, or alkyllithium reagent to form the corresponding tertiary alcohol.

Claim 42 (Original): The method of claim 37 wherein the trioxolane has an ester functional group, and is treated with a reducing agent to form an alcohol.

Claim 43 (Original): The method of claim 42 whereby the trioxolane is selected from the group consisting of OZ70 and OZ61.

Claim 44 (Original): The method of claim 43 whereby OZ70 is treated with a reducing agent to form OZ119.

Claim 45 (Original): The method of claim 43 whereby OZ61 is treated with a reducing agent to form OZ89.

Claim 46 (Original): The method of claim 39 wherein the trioxolane has an ester functional group, and is treated with a hydrolyzing agent to form an acid.

Claim 47 (Original): The method of claim 46 wherein the hydrolyzing agent is aqueous potassium hydroxide.

Claim 48 (Original): The method of claim 46 wherein OZ61 is treated with a hydrolyzing agent to form OZ78.

Claim 49 (Currently Amended): The method of claim [[35]]57 wherein the trioxolane has ~~an~~ a phthalimide functional group, and is treated with a deprotecting reagent to form an amine.

Claim 50 (Original): The method of claim 49 whereby the phthalimide is selected from the group consisting of OZ136, OZ146, and OZ167.

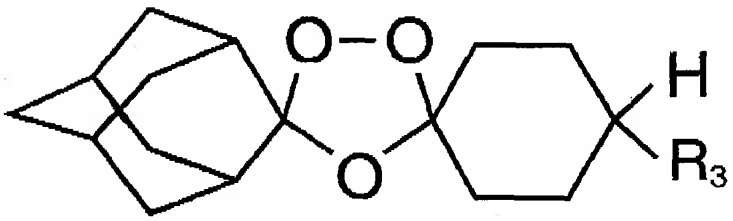
Claim 51 (Original): The method of claim 50 whereby OZ136 is treated with a deprotecting reagent to form OZ137.

Claim 52 (Original): The method of claim 50 whereby OZ146 is treated with a deprotecting reagent to form OZ181.

Claim 53 (Original): The method of claim 52 whereby OZ167 is treated with a deprotecting reagent to form OZ269.

Claim 54 (Original): The method of claim 53 wherein the deprotecting reagent is hydrazine.

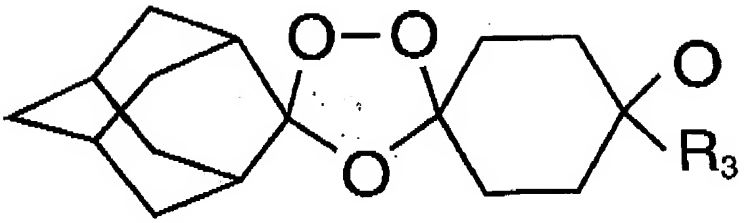
Claim 55 (Original): A spiro or dispiro 1,2,4-trioxolane having the following structure:



whereby R_3 is $(CH_2)_n$-Y, and further providing that Y is a weak base amide; and n is an integer.

Claim 56 (Original) The trioxolane of claim 55 whereby n = 1.

Claim 57 (New) A method of synthesizing a dispiro 1,2,4-trioxolane comprising: treating a trioxolane having the following structure:



wherein R_3 is selected from the group consisting of a ketone, an aldehyde, an ester, and a phthalimide with one or more reagents selected from the group consisting of an oxidizing agent, reducing agent, hydroxylamine, hydrazine, diol, alcohol, heteroaryllithium, aryllithium, alkyllithium, hydrolyzing agent, and deprotecting agent to form a compound selected from the group consisting of lactone, alcohol, oxime ether, hydrazone, ketal, acetal, amine, and acid.